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DOES BOMBESIN MEDIATE STRESS-RESPONSE THROUGH CRF RELEASE? EFFECTS OF BN ON BRAIN CRF, PLASMA ACTH, CORTICOSTERONE AND CATECHOLAMINES. P. Kent[1] and Z. Merali[1,2]. [1]School of Psychology and [2]Dept. of Pharmacology, University of Ottawa, Ontario, Canada.

A characteristic response to stress involves the coincident activation of the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system. Activation of these systems results in specific endocrine and autonomic changes including increased plasma ACTH, corticosterone, norepinephrine, epinephrine and glucose levels. Current research indicates that many of these effects are mediated by corticotropin-releasing factor (CRF). It has already been established that central injections of the neuropeptide Bombesin (BN) elicits behaviors typically associated with increased emotionality and arousal such as increased grooming, shuttle escape deficits and suppression of food intake. Moreover, recent results from our laboratory have shown that stress alters levels of BN-like peptides in several brain regions. The objective of the current investigation was to elucidate the relationship between BN-like peptides and CRF. Results from our first experiment demonstrate that the central administration of BN (0.25 and 0.5 μg/3 μl), like CRF, caused a significant dose-dependent increase in plasma levels of ACTH, corticosterone, norepinephrine, epinephrine and glucose, 20 min post injection. Pretreatment with the CRF antagonist, αhCRF (10 μg/3 μl), significantly attenuated the BN-induced increases in plasma ACTH, norepinephrine, epinephrine and glucose, but had little or no effect on plasma corticosterone levels at this time point. The second experiment examined changes in CRF immunoreactivity in various brain regions 20 min following i.c.v. administration of BN (0.25 and 0.5 μg/3 μl). A significant reduction in CRF immunoreactivity was found in the amygdala, the anterior and ventromedial hypothalamic nuclei and the nucleus of the solitary tract. A trend towards a reduction in CRF immunoreactivity was observed in the median eminence, the lateral hypothalamus, the hippocampus and the prefrontal cortex, whereas no significant changes were found in the paraventricular or the dorsomedial nucleus of the hypothalamus. Taken together, these results suggest that 1) BN-like peptides may play a role in the mediation or modulation of stress response and 2) that some of these effects may be mediated via modulation of CRF release.

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THE ACTIONS OF GALANIN AND M40 ON DELAYED NON-MATCHING TO POSITION IN ^{192}IgG-SAPORIN-LESIONED RATS. M.P. McDonald[1], G.L. Wenk[2], & J.N. Crawley[1]. [1]Section on Behavioral Neuropharmacology, ETB, NIMH, Bethesda, MD 20892, and [2]Division of Neural Systems, Memory and Aging, University of Arizona, Tuscon, AZ 85724.

Galanin is a 29-amino acid neuropeptide that coexists with acetylcholine (ACh) in the medial septum/diagonal band in the rat and inhibits acetylcholine release in the septohippocampal pathway. Galanin is overexpressed in the basal forebrain in Alzheimer's disease (AD). Galanin impairs performance on several rodent learning and memory tasks, including delayed non-matching to position (DNMTP). M40 (galanin[1-12]-Pro$_3$-(Ala-Leu)$_2$-Ala-NH$_2$), a peptidergic galanin receptor ligand, has previously been shown to antagonize galanin-induced impairment on DNMTP. The current experiments used a lesion model of AD to evaluate the actions of galanin and M40 on DNMTP when cholinergic transmission was reduced. Rats were injected with ^{192}IgG-saporin, an immunotoxin that selectively lesions cholinergic cells in the basal forebrain and produced a 54% reduction in hippocampal choline acetyltransferase in the present study. After recovery, rats were injected with galanin in the lateral ventricle and with M40 in the lateral ventricle or the ventral hippocampus. Galanin treatment significantly reduced choice accuracy in both the lesioned and sham groups. M40 along did not affect choice accuracy. These results suggest that blocking endogenous galanin is not sufficient alone to improve performance in lesioned rats, indicating the potential need for a combined cholinergic-galaninergic treatment strategy.